Examiner's contention and reserve the right to take a contrary position in this application and in any future related patent applications. The Examiner's claim objections and rejections are overcome or traversed as set forth below.

I. TRAVERSE OF THE ANTICIPATION REJECTIONS

A. Traverse Of The WO 97/16452 Rejection

The Examiner rejected claims 50-54, 58-62, 66, 72, 79-83, 85 and 87-90 for being anticipated by WO 97/16452.

The Examiner's rejection has been overcome by amending all relevant claims so that R_1 does not include substituted aryl as a substituent. This amendment renders all pending application claims novel over WO 97/16452.

B. Traverse Of The Schow Rejections

The Examiner rejected claims 50-57, 60-61, 63-65, 67-71, 73-75, 79-83, 85 and 87-90 for being anticipated by Schow.

The Examiner's rejection has been overcome by adding a proviso to claim 50 that excludes compounds 9 and 14 of the Schow reference from the claimed compounds.

C. Traverse Of The U.S. Patent No. 5,866,702 Rejection

The Examiner rejected claims 50-72, 76-83, 85 and 87-90 as being anticipated by U.S. Patent No. 5,866,702.

This novelty rejection is improper because the '702 patent is not prior art under 35 USC 102(a). The '702 patent became prior art under 102(a) on February 2, 1999, one day after the February 1, 1999 filing date of the immediate parent of this application. As a result, the '702 patent is not available to the Examiner as 102(a) prior art, and the Examiner's novelty rejection on the basis of the '702 patent should be withdrawn.

II. TRAVERSE OF THE OBVIOUSNESS REJECTION

The Examiner rejected claims 50-57, 60-61, 63-65, 67-71, 73-75, 79-83, 85 and 87-90 as being unpatentable for obviousness over the Meijer patent.

The Examiner's obviousness rejection is improper. The Examiner's rejection is based on mixing and matching the various substituents listed in Table I of Meijer to obtain several of the claimed compounds. The Examiner's rejection is based upon improper hindsight consideration of Table I with the Applicant's invention in mind. The Examiner has not pointed to any teaching or suggestion in Meijer that the various substituents listed in Table I can be mixed and matched as the Examiner suggests. Without such a teaching or suggestion, the Examiner's obviousness rejection must be withdrawn.

III. THE OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION

The Examiner rejected claims 50-90 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 48-74 and 76 of co-pending application number 09/929,771.

The Applicants are prepared to file a Terminal Disclaimer to overcome the Examiner's claim rejections should any claim of either application be allowed by the Examiner.

IV. TRAVERSE OF THE 35 U.S.C. 112, FIRST PARAGRAPH REJECTION

A. The Rejection Of Claims 50-67, 72 And 77-79

The Examiner rejected claims 50-67, 72, and 77-90 because the third proviso lacks a description in the specification and because the use of the term "and" in the claim is unclear.

Page 12, line 8-10 of the specification recites the proviso in question. It is clear from the proviso in the specification that the word "and" is properly used before the term "R_2" in the claims. The provisos all list combinations of R_1, R_2, and R_3 substituents that are excluded from the claimed compounds. To read the third proviso to contain any other word than "and" would be contrary to common sense. Thus, it is the Applicant's position that the third proviso is enabled by the specification.

B. The Remaining 112, First Paragraph Rejections

The Examiner rejected Claims 81-85, 87 and 90 under 35 U.S.C. 112, first paragraph, alleging that:

> The compounds are disclosed to be CDK2 inhibitors. There is no reason to think that one of ordinary skill in the art could, without undue experimentation, treat such difficult disorders with such compounds.

Applicants respectfully traverse the rejection.

As an initial matter, Applicants point out that the Examiner does not identify which disorders he believes to be "difficult". Some of them? All of them? Presumably the Examiner does not doubt that Applicants' compounds of the invention are CDK2 inhibitors. This is well established in Example 7 of the application.

In any event, it is well known that CDK2 inhibitors have the spectrum of activity disclosed by Applicants. The acronym CDK stands for "Cyclin Dependent Kinase". It is well established that cell division is controlled in eukaryotes by Cyclin Dependent Kinases; see, for example, Trends Cell Biology (1997), 7(3), 95-98. Cyclins, and their

effector counterpart, the CDKs, are regulatory proteins, the aberrant expression of which has been associated with a variety of human cancers; see, for example, Current Pharmaceutical Design (2000), 6(4), 379-392. Thus, inhibition of such aberrant expression of the cyclins is a target for novel anticancer agents, such as those of Applicants' invention.

The Examiner additionally states that:

> For example, Vesely says, "It is possible that, through its specificity, olomoucine may lead to a compound which will preferentially inhibit the proliferation of certain tumor cells." Olomoucine is excluded by proviso from the claims. This shows that basic research is still required to obtain the necessary selectivity. Abraham says that "olomoucine may constitute a lead compound for the design of new anti-tumor agents." Similarly, Schultz-Gahmen referring to its results, says it "should prove useful in modifying and improving the lead compounds." But a lead compound is one which is not actually ready for use; it its by its nature something which needs to be modified by additional research."

Applicants submit that there is no requirement that a compound claimed in a patent application be "ready for use". If such a requirement existed there would be very few patented compounds. Additionally, Applicants know of no definition of a lead compound as "something which needs to be modified by additional research". It is not. A lead compound is one developed by research that shows promise for a specific utility. Further examination of the compound may show it to be valuable as such for development as a marketable entity, or indeed other compounds may be derived from the lead compound. However, as stated above, there is no provision under U.S. patent law that requires certainty as to being "ready for use". All that is required is that the patent specification teaches how to make the compounds of the invention, and how to use them to treat proliferative disorders. "It is not fatal if some experimentation is needed, for the

patent document is not intended to be a production specification". *Northern Telecom, Inc. v. Datapoint Corp.*, 15 USPQ1321, 1329 (Fed. Cir. 1990). (See also *In re Gay*, 135 USPQ at 316; *Atlas Powder Co. v . E.I. Du pont De Nemours and Co.*, 224 USPQ 409 (Fed. Cir. 1984).

Applicants agree with the Examiner's statement that "Olomoucine is excluded by proviso from the claims." Olomoucine is excluded from the instant claims, of course, because it is not a compound of Applicants' invention, and thus the Examiner's conclusion that "this shows that basic research is still required to obtain the necessary selectivity" is in error.

Applicants respectfully submit that the Vesely citation is taken out of context. Vesely also states that "[T]he unusual specificity of olomoucine toward cell cycle controlling enzymes suggests that olomoucine could be used to inhibit specifically certain steps of the cell cycle." The Examiner's conclusion that "olomoucine itself is not potent enough to be effective" is incorrect, for several reasons. For example, potency is not the only measure of effectiveness of a compound as a drug. Other important characteristics of a drug are selectivity, bioavailability, efficacy, stability, and the like. Additionally, as stated above, there is no provision under U.S. patent law that requires certainty as to a claimed compound being "ready for use". All that is required is that the patent specification teaches how to make the compounds of the invention, and how to use them to treat proliferative disorders. All of this has been demonstrated.

Applicants respectfully submit that the rejection of Claims 81-85, 87 and 90 under 35 U.S.C. 112, first paragraph, should be withdrawn.

The Examiner rejected Claims 83 and 85 under 35 U.S.C. 112, first paragraph, alleging that:

> "Claims 83 and 85 call for the treatment of cancer in general. However, there never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancers, but no one has ever been able to figure how to get a compound to be effective against cancer generally, or even a majority of cancers."

Cancer is due to a breakdown in the regulatory pathways that control the cell cycle. Most cancer chemotherapies have utilized this general principle to devise treatments for tumors. They are almost all non-selective inhibitors of growth of any dividing cell. Thus, cisplatin, ardriamycin, alkylating agents , antimetabolites, and the like have all been used to treat more than one type of cancer. The compounds provided by Applicants' invention are effective at inhibiting the proliferation of many kinds of cells, and thus would be recognized by those skilled in the art as effective anti-tumor agents. Consequently, Applicants request that the rejection of Claims 83 and 85 be withdrawn.

The Examiner rejected Claim 81 under 35 U.S.C. 112, first paragraph, alleging that:

> "Further, claim 81 is even broader, covering presumably any cell proliferative disorder. A proliferative disorder is anything that causes abnormal tissue growth. That can be growth by cellular proliferation more rapidly than normal, or continued growth after the stimulus that initiated the new growth has ceased, or lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such a term covers not only all cancers, but also covers pre-cancer conditions such as lumps, lesions, and polyps. In addition, it embraces various non-cancerous proliferative disorders such as certain types of restenosis, vascular smooth muscle proliferation associated with atherosclerosis, glomerular nephritis, clonal proliferative disorders including the various myelodysplastic syndromes, such as refractory anemias, certain types of abnormal wound healing, different types of abnormal angiogenesis, pulmonary fibrosis, macular degeneration, meyeloproliferative disorders such as primary polycythemia and myelofibrosis, and rheumatoid arthritis. There is no such thing that an

agent which is effective against such disorders generally, since they are so diverse, nor is there any reason to think that such an agent could be made to work."

Abnormal tissue growth is due to the uncontrolled growth of cells that make up the tissues. The proliferation of cells is controlled by regulatory enzymes. The basic mechanisms of enzymatic control are alike in all cells. Thus, these proliferative diseases share a basic mechanistic abnormality that culminates in hyperproliferation. As described in the specification, the invention consists of compounds that inhibit CDK-2 and IkB-a. These two enzymes regulate the cell cycle in a wide variety of cells. Inhibition of these enzymes will modulate the replication of all the cells described.

For example, rheumatoid arthritis (RA) is an inflammatory disease cause by the excessive proliferation of cells that secrete pro-inflammatory cytokines. Inhibition of the proliferation of these cells decreases the number of cells producing these cytokines. Inhibition of the proliferation of proinflammatory leukocytes is the basis for a variety of treatments for RA. A treatment for RA is cyclophosphamide, a cytotoxic drug which is also used to treat cancer (Chemotherapy of Neoplastic Diseases, 1995. (Gilbert and Goodman, The Pharmacological Basis of Therapeutics, Chapter 51, p. 1239, McGraw-Hill).

Systemic lupus erthematosis (lupus) is a disorder beginning with an immunological response that stimulates the proliferation of fibroblasts. The fibroblasts, in turn, secrete excessive collagen, which results in the clinical manifestations of the disease. Treatments for lupus include methotrexate, another anti-neoplastic drug, which is cytotoxic to cells. Methotrexate is used to proliferative disorders, including lupus and psoriasis, in addition to cancer (Chemotherapy of Neoplastic Diseases, 1995, Gilbert and

Goodman's The Pharmacological Basis of Therapeutics, Chapter 51, p. 1246. McGraw-Hill.)

Multiple sclerosis (MS) is an autoimmune disorder characterized by the proliferation of auto-reactive T cells that attack myelin. One of the methods of treating MS is treatment with agents that inhibit the proliferation of the T-cell clones, i.e., with immunosuppressives. In addition to methotrexate and cyclophosphamide, chlorambucil, vincristine, vinblastine and dactinomycin are used to treat both cancer and immunoproliferative disorders (Drugs used for Immunodulation, 1995, Gilbert and Goodman, The Pharmacological Basis of Therapeutics, Chapter 52, p. 1239, McGraw-Hill). Cancer, which can occur in most tissues, is due to a breakdown in the normal regulatory pathways of the cell cycle.

The Examiner also rejected Claim 81 because "it covers healthy processes as well." While not necessarily agreeing with the Examiner Applicants have amended the claim to further clarify the invention.

Examiner stated that "the inclusion of gout in claim 83 makes no sense at all. Patients with gout are normally told to avoid high purine foods, in order to reduce uric acid secretion." In fact, patients with gout often have an inflammatory lesion resulting from the crystals of uric acid. The inflammation, like any other inflammation, may be treated with any agent that reduces the number of proliferating clones of immunocytes. Therefore, compounds that inhibit CDK-2 and IkB-a-kinases will inhibit the growth of populations of cells.

The Examiner also states that

"Lupus and MS in Claim 71 are intractable nervous system disorders that "no one has been able to treat these with CDK2 inhibitors.

Lupus and MS are autoimmune disorders. Lupus is a generalized connective tissue disorder (Dorland's Illustrated Medical Dictionary). In lupus the proliferation of autoreactive T cell clones stimulates the division of fibroblasts, which are connective tissue cells. The fibroblasts secrete collagen, a connective tissue protein, in abnormally high amounts. Lupus has been treated as described above with anti-neoplastic agents that inhibit cell growth. CDK2 inhibitors also inhibit cell growth.

MS is an autoimmune disorder in which clones of autoreactive T cells mount an immune response to myelin. WO 0055161 discloses biarylmethylaminopurines as potent cyclin/CDK inhibitors and antiproliferative agents. Furthermore their use in the treatment of rheumatoid arthritis, lupus, type 1 diabetes, multiple sclerosis, cancer, restenosis, gout, and other proliferative diseased is disclosed.

Applicants respectfully submit that the claimed disorders are all cell proliferative disorders, and accordingly this rejection should be withdrawn.

V. TRAVERSE OF THE 35 USC SECOND PARAGRAPH REJECTIONS

The Examiner rejected claims 50-90 under USC 112 second paragraph. The Examiner's claim rejections are overcome or traversed as set forth below.

1. This rejection has been overcome by amending claim 50 as suggested by the Examiner.

2. This rejection has been overcome by amending claim 50 as suggested by the Examiner.

3. This rejection has been overcome by amending claim 50 to convert the subscripts into superscripts. The proviso, which includes the objectionable claim term, has been removed from all dependent claims as redundant.

4. In the context of the claimed invention, the term substituted includes the possibility that hydrogen is the selected substituent. Therefore, the possibility that R_2 is hydrogen is not an error.

5. The Examiner stated that the term "acyl" is indefinite. The Examiner's attention is drawn to the specification on page 19, lines 11-12 where the term "acyl" is defined as

> "acyl" denotes groups –C(O)R, where R is hydrogen, lower alkyl, substituted lower alkyl, aryl, substituted aryl and the like as defined herein.

The Applicants definition of acyl definitively establishes the scope of the substituent and the Examiner's rejection should be withdrawn.

6. See the Applicants' Response in paragraph 5 above.

7. The Examiner asserts that the term "heteroaryl" and "heterocyclyl" are redundant. The substituents "heteroaryl" and "heterocyclyl" are defined differently in the specification with the substituent "heterocyclyl" being specifically defined as a non-aromatic moiety. For this reason, the terms are not redundant and should be allowed to remain together in the claims.

8. The term "heterocyclic" is not used in the application specification or claims. The Applicants use the term "heterocyclyl" or "heterocycle" to define certain substituents. Both of these terms are defined in the specification in a manner that establishes their scope.

9. The Examiner's rejection has been overcome by amending claim 50 to delete the word "each" in the objectionable term. The claim now allows the substituent to have from 1 to 20 carbon atoms. It would be within the knowledge of one skilled in the art what range of carbon atoms would apply to the various potential substituents.

10. The Examiner's rejection has been overcome by amending claim 55 to include substituted substituents in the list of potential substituents.

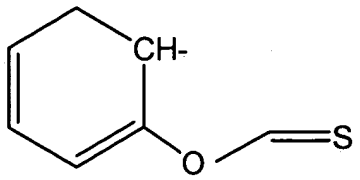
11. The claims have been amended as suggested by the Examiner.

12. The Examiner alleges that the term "amide" is indefinite. The term "amide" is always used in the specification and claims in the term "heteroaryl amide." The term "heteroaryl amide" is not indefinite.

13. The Examiner's rejection has been rendered moot by the canceling the redundant proviso from all dependent claims in which it appears.

14. The Examiner's objection to claim 81 has been overcome by amending claim 81 such that it is now directed to "A method for treating a disease state that is characterized by abnormal cell proliferation …. "

15. The term "thiomethoxyphenyl" refers to the following substituent:



16. The term "cycloalkyl" and "substituted cycloalkyl" in claim 61 fall within the scope of the definition of the term "alkyl" and "substituted alkyl". Therefore, the terms "cycloalkyl" and "substituted cycloalkyl" rely on the terms alkyl and substituted alkyl in claim 61 for their antecedent basis.

17. The preamble of Claim 50 has been amended to include compounds and salts thereof in order to provide antecedent basis for claims 79-80.

18. The term "cationic salt" is defined in the specification at page 24, lines 15-20.

19. The Examiner's objection has been overcome by canceling the word "from" where it appears before the number 1 in Claim 63.

20. The Applicants traverse the rejection of Claim 83 because "host graft disease" is defective. Host graft disease is the well known phenomenon of graft rejection. Graft v. host disease is a related disorder in which T-lymphocytes passively transferred by the donor graft mount an adverse immunological response to the recipient's tissues. Both disorders involve the unwanted proliferation of T-lymphocytes.

21. The rejection has been overcome by amending the claim as suggested by the Examiner.

22. The rejection has been overcome by amending the claim as suggested by the Examiner.

23. The rejection has been overcome by canceling the term "R^{22}" from the objectionable claim.

24. The rejection of claim 89 has been overcome by canceling claim 89 from the application and replacing it with new claim 91.

25. The Examiner has objected to the use of the term "substituted acyl" because it makes no sense. The term "substituted acyl" is definite because it distinguishes acyl substituents that are substituted with an one or more additional substituents from acyl substituents that are unsubstituted.

26. The rejection has been overcome by inserting the letter "c" into the composition name.

27. Applicants traverse the rejection of Claim 83. Gout is a manifestation of hyperuricemia as the Examiner suggests. Also, crystals of sodium urate cause acute inflammatory arthritis. The Examiner maintains that gout is not treated with antiproliferative agents but with anti-inflammatory agents. Inflammation is caused by the proliferation of clones of immunoreactive T cells. Consequently, inhibition of the proliferation of these cells is a method of treating the symptoms of Gout. Additionally, many anti-inflammatory agents are anti-proliferative agents.

The Examiner also maintains that multiple sclerosis is of unknown cause. Multiple sclerosis is due to the destruction of myelin by autoreactive cells. Thus, multiple sclerosis is an autoimmune disorder. Treatment of multiple sclerosis frequently employs agents that quell the proliferation of T-lymphocytes.

As the Examiner suggests, SLE is due to the hyperactivity of the immune system. The basis of the hyperactivity of the immune system is the proliferation of immunocytes. Proliferation of cell populations is almost always a sequela of an immune response. Consequently, the inhibition of these clones abrogates the detrimental immune response in immunologically based orders such as SLE.

Host graft disease is another immunological disorder in which the host mounts an undesired response to donor tissue. Again, immunological responses involve the proliferation of immunocytes. In this case proliferation of helper T lymphocytes populations produces the disorder. In graft versus host disease the same thing occurs but

in this case it is T-cells contained in the graft that mounts a response to the recipients tissues.

Type I diabetes is, as the Examiner suggests, an autoimmune disorder. Autoimmune disorders are caused by the proliferation of autoreactive T lymphocyte clones against "self-antigens" in affected individuals.

Restinosis is exactly a proliferative disorder. In restinosis, intimal smooth muscle proliferates, resulting in occlusion of the vessel.

28. The rejection has been overcome by canceling the first substituent listed in claim 78.

29. The rejection of claim 29 has been overcome by amending claim 78 to be dependent upon claim 60.

30. The rejection of claim 60 is rendered moot by the previously described cancellation of the proviso from the claims.

31. The Examiner is unclear about the last phrase in Claim 90. Specifically, he rejects the expression cancers derived from endothelial cells. While not necessarily agreeing with the Examiner Applicants have amended Claim 90 to better characterize the invention.

VI. THE SPECIFICATION OBJECTION

A. The Application Priority Data

The specification has been amended to correctly recite the application priority data.

B. The Application Abstract

The application Abstract has been amended to overcome the Examiner's rejection

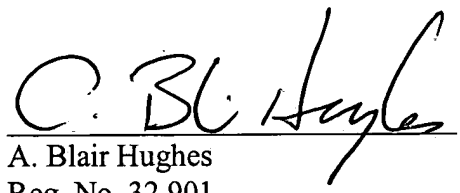
C. The Synthesis Schemes

The Examiner objected to the synthesis scheme on page 28 of the specification for failure to recite the reagent used. The synthesis scheme is sufficient to enable one skilled in the art to manufacture the claimed compounds. Therefore, the Applicant's do not believe that any change to the scheme is required.

Favorable consideration and early allowance of pending application claims 50-88 and 90-91 is courteously solicited.

McDonnell Boehnen Hulbert & Berghoff

Respectfully submitted,

By: 

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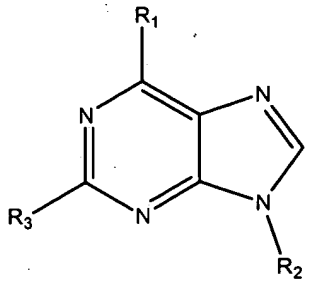
Dated: July 10, 2002

APPENDIX A
Marked Up Claims Pursuant To 37 CFR 1.121

IN THE CLAIMS:

50. (Once amended) A 2,6,9-trisubstituted purine composition of matter and salts thereof having the following formula:



wherein R_1 is halogen or R'_1-X wherein X = NH, O, S, $S(O_2)$[.];

R'_1 is alkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, each having one to 20 carbon atoms, which alkyl, heterocyclyl, [aryl,] heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 3 substituents independently selected from the group consisting of halo, aryl, CF_3, heteroaryl, heterocyclyl, [R^{22},] SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $SO_2NR^{20}COR^{21}$, $SO_2NR^{20}CONR^{20}R^{23}$, $SO_2NR^{20}CO_2R^{21}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}CONR^{20}R^{23}$, $N(R^{20})C(NR^{20})NHR^{23}$, $NR^{20}SO_2R^{21}$, OR^{20}, $OCONR^{20}R^{23}$, $OCONR^{20}SO_2R^{21}$, $OCONR^{20}R^{23}$, CN, CO_2R^{20}, $CONR^{20}R^{23}$, $CONR^{20}SO_2R^{21}$ and COR^{20};

R_2 is a hydrogen or hydrocarbon selected from the group alkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, each having one to 20 carbon atoms, which alkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 3 substituents independently selected

from the group consisting of halo, aryl, heteroaryl, heterocyclyl, [R^{22},] SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $SO_2NR^{20}COR^{21}$, $SO_2NR^{20}CONR^{20}R^{23}$, $SO_2NR^{20}CO_2R^{21}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}CONR^{20}R^{23}$, $N(R^{20})C(NR^{20})NHR^{23}$, $NR^{20}SO_2R^{21}$, OR^{20}, $OCONR^{20}R^{23}$, $OCONR^{20}SO_2R^{21}$, $OCONR^{20}R^{23}$, CN, CO_2R^{20}, $CONR^{20}R^{23}$, $CONR^{20}SO_2R^{21}$ and COR^{20};

R_3 is $-NR_4R_5$, wherein R_4 and R_5 are each independently hydrogen, or a hydrocarbon selected from the group [including]consisting of alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, [each] having one to 20 carbon atoms, which alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 3 substituents independently selected from the group consisting of halo, aryl, heteroaryl, heterocyclyl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $SO_2NR^{20}COR^{21}$, $SO_2NR^{20}CONR^{20}R^{23}$, $SO_2NR^{20}CO_2R^{21}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}CONR^{20}R^{23}$, $N(R^{20})C(NR^{20})NHR^{23}$, $NR^{20}SO_2R^{21}$, OR^{20}, $OCONR^{20}R^{23}$, $OCONR^{20}SO_2R^{21}$, $OCONR^{20}R^{23}$, CN, CO_2R^{20}, $CONR^{20}R^{23}$, $CONR^{20}SO_2R^{21}$ and COR^{20}, with the proviso that either R_4 or R_5 must be substituted with [$NR_{20}R_{23}$] $NR^{20}R^{23}$, and [wherein when R_3 is 2-hydroxyethylamino and R_2 is methyl then R_1'-X is not amino, 3-methyl-2-butenylamino, benzylamino, or m-hydroxybenzylamino, and wherein] when R_3 is not 2-hydroxyethylamino and R_2 is isopropyl, then R_1'-X is not benzylamino, m-hydroxybenzylamino, or 3-methylbutylamino, and wherein [when R_3 is 2-hydroxyethylamino and R_2 is 2-hydroxyethyl, then R_1'-X is not benzylamino, and wherein] when R_3 is selected from [the group consisting of 2-methyl-2-hydroxypropylamino and] 2-dimethylaminoethylamino, and when R_2 is methyl, then R_1'-

X is not benzylamino, and wherein when R_1' is 4-methoxybenzylamino and R_2 is isopropyl, then R_3 is not 2-aminoethylamino or 2-aminomethylethanolamino;

R^{20} is a member selected from the group consisting of H, C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, heterocyclyl, aryl, and heteroaryl, which alkyl, alkenyl, alkynyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl or heteroaryl amide, CN, O-C_{1-6} alkyl, CF_3, aryl, and heteroaryl;

R^{21} is a member selected from the group consisting of C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, heterocyclyl, aryl, and heteroaryl, which alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from the group of halo, heterocyclyl, aryl, heteroaryl, CF_3, CN, OR^{20}, SR^{20}, $N(R^{20})_2$, $S(O)R^{22}$, SO_2R^{22}, $SO_2N(R^{20})_2$, $SO_2NR^{20}COR^{22}$, $SO_2NR^{20}CO_2R^{22}$, $SO_2NR^{20}CON(R^{20})_2$, $N(R^{20})_2$ $NR^{20}COR^{22}$, $NR^{20}CO_2R^{22}$, $NR^{20}CON(R^{20})_2$, $NR^{20}C(NR^{20})NHR^{23}$, COR^{20}, CO_2R^{20}, $CON(R^{20})_2$, $CONR^{20}SO_2R^{22}$, $NR^{20}SO_2R^{22}$, $SO_2NR^{20}CO_2R^{22}$, OR^{20}, $OCONR^{20}SO_2R^{22}$, $OC(O)R^{20}$, $C(O)OCH_2OC(O)R^{20}$, and $OCON(R^{20})_2$, and each optional heteroaryl, aryl, and heterocyclyl substituent is optionally substituted with halo, alkyl, CF_3, amino, mono- or di- alkylamino, alkyl or aryl or heteroaryl amide, $NCOR^{22}$, $NR^{20}SO_2R^{22}$, COR^{20}, CO_2R^{20}, $CON(R^{20})_2$, $NR^{20}CON(R^{20})_2$, $OC(O)R^{20}$, $OC(O)N(R^{20})_2$, SR^{20}, $S(O)R^{22}$, SO_2R^{22}, $SO_2N(R^{20})_2$, CN, or OR^{20};

R^{22} is a member selected from the group consisting of C_{1-15} alkyl, C_{2-15} alkenyl, C_{2-15} alkynyl, heterocyclyl, aryl, and heteroaryl, which alkyl, alkenyl, alkynyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents

independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl or heteroaryl amide, CN, O-C_{1-6} alkyl, CF_3, aryl, and heteroaryl; and

R^{23} is R^{21} or H.

51. (Once amended) A 2,6,9-trisubstituted purine composition of claim 50 wherein:

R'_1 is a alkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, each having one to 20 carbon atoms, which alkyl, heterocyclyl, [aryl,] heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 3 substituents independently selected from the group consisting of halo, CF_3, aryl, heteroaryl, heterocyclyl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}CONR^{20}R^{23}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, $CONR^{20}R^{23}$, and COR^{20};

R_2 is a hydrogen or hydrocarbon selected from the group substituted alkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, each having one to 20 carbon atoms, which alkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 3 substituents independently selected from the group consisting of halo, aryl, heteroaryl, heterocyclyl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}CONR^{20}R^{23}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, $CONR^{20}R^{23}$, and COR^{20};

R_4 and R_5 are each independently hydrogen, or a hydrocarbon selected from the group [including]consisting of alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, each having one to 20 carbon atoms, which alkyl,

acyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 3 substituents independently selected from the group consisting of halo, aryl, heteroaryl, heterocyclyl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}CONR^{20}R^{23}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, $CONR^{20}R^{23}$, and COR^{20} [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, $C_{1\text{-}8}$alkyl, $C_{2\text{-}8}$ alkenyl, $C_{2\text{-}15}$ heterocyclyl, aryl, and heteroaryl, which alkyl, alkenyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl or heteroaryl amide, CN, O-$C_{1\text{-}6}$ alkyl, CF_3, aryl, and heteroaryl;

R^{21} is a member selected from the group consisting of $C_{1\text{-}8}$ alkyl, $C_{2\text{-}8}$ alkenyl, heterocyclyl, aryl, and heteroaryl, which alkyl, alkenyl, aryl, heterocyclyl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from the group of halo, heterocyclyl, aryl, heteroaryl, CF_3, CN, OR^{20}, SR^{20}, $N(R^{20})_2$, $S(O)R^{22}$, SO_2R^{22}, $SO_2N(R^{20})_2$, $SO_2NR^{20}COR^{22}$, $SO_2NR^{20}CO_2R^{22}$, $SO_2NR^{20}CON(R^{20})_2$, $N(R^{20})_2$ $NR^{20}COR^{22}$, $NR^{20}CO_2R^{22}$, $NR^{20}CON(R^{20})_2$, $NR^{20}C(NR^{20})NHR^{23}$, COR^{20}, CO_2R^{20}, $CON(R^{20})_2$, $CONR^{20}SO_2R^{22}$, $NR^{20}SO_2R^{22}$, $SO_2NR^{20}CO_2R^{22}$, OR^{20}, $OCONR^{20}SO_2R^{22}$, $OC(O)R^{20}$, $C(O)OCH_2OC(O)R^{20}$, and $OCON(R^{20})_2$, and each optional heteroaryl, aryl, and heterocyclyl substituent is optionally substituted with halo, alkyl, CF_3, amino, mono- or di- alkylamino, alkyl or aryl or heteroaryl amide, $NCOR^{22}$, $NR^{20}SO_2R^{22}$, COR^{20}, CO_2R^{20}, $CON(R^{20})_2$, $NR^{20}CON(R^{20})_2$, $OC(O)R^{20}$, $OC(O)N(R^{20})_2$, SR^{20}, $S(O)R^{22}$, SO_2R^{22}, $SO_2N(R^{20})_2$, CN, or OR^{20}; and

R^{22} is a member selected from the group consisting of C_{1-8} alkyl, C_{2-8}alkenyl, heterocyclyl, aryl, and heteroaryl, which alkyl, alkenyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl or heteroaryl amide, CN, O-C_{1-6} alkyl, CF_3, aryl, and heteroaryl.

52. (Once amended) A 2,6,9-trisubstituted purine composition of claim 50 wherein:

R'_1 is alkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, each having one to 20 carbon atoms, which alkyl, heterocyclyl, [aryl,] heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 3 substituents independently selected from the group consisting of halo, CF_3, aryl, heteroaryl, heterocyclyl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, $CONR^{20}R^{23}$, and COR^{20};

R_2 is a hydrogen or hydrocarbon selected from the group [including]consisting of alkyl, heterocyclyl, and aryl, each having one to 10 carbon atoms, which alkyl, heterocyclyl, aryl, are optionally substituted with from 1 to 3 substituents independently selected from the group consisting of halo, aryl, heteroaryl, heterocyclyl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, $CONR^{20}R^{23}$, and COR^{20};

R_4 and R_5 are each independently hydrogen, or a hydrocarbon selected from the group [including]consisting of alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, alkenyl, and alkynyl, each having one to 20 carbon atoms, which alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 3

substituents independently selected from the group consisting of halo, aryl, heteroaryl, heterocyclyl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, $CONR^{20}R^{23}$, and COR^{20} [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, $C_{1\text{-}8}$alkyl, aryl, and heteroaryl, which alkyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl or heteroaryl amide, CN, O-$C_{1\text{-}6}$ alkyl, CF_3;

R^{21} is a member selected from the group consisting of $C_{1\text{-}8}$ alkyl, aryl, and heteroaryl, which alkyl, aryl, and heteroaryl are optionally substituted with 1 to 2 substituents independently selected from the group of halo, CF_3, CN, OR^{20}, SR^{20}, $N(R^{20})_2$, $S(O)R^{22}$, SO_2R^{22}, $SO_2N(R^{20})_2$, $NR^{20}CO_2R^{22}$, $NR^{20}CON(R^{20})_2$, COR^{20}, CO_2R^{20}, $CON(R^{20})_2$, $NR^{20}SO_2R^{22}$, OR^{20}; and

R^{22} is a member selected from the group consisting of $C_{1\text{-}8}$ alkyl, aryl, and heteroaryl, which alkyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl or heteroaryl amide, CN, O-$C_{1\text{-}6}$ alkyl, CF_3, aryl, and heteroaryl.

53. (Once amended) A 2,6,9-trisubstituted purine composition of claim 50 wherein:

R'_1 is a alkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, each having one to 20 carbon atoms, which alkyl, heterocyclyl, [aryl,] heteroaryl, aralkyl, heteroarylalkyl, alkenyl, and alkynyl, are optionally with from 1 to 2 substituents independently selected from the group consisting of halo, CF_3,, aryl, R^{22},

SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, and $CONR^{20}R^{23}$;

R_2 is a hydrogen or hydrocarbon selected from the group alkyl, heterocyclyl, and aryl, each having one to 10 carbon atoms , which alkyl, heterocyclyl, aryl, are optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, aryl, heteroaryl, heterocyclyl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, $CONR^{20}R^{23}$, and COR^{20};

R_4 and R_5 are each independently hydrogen, or a hydrocarbon selected from the group [including]consisting of alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, alkenyl, and alkynyl, each having one to 20 carbon atoms, which alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, aryl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, and $CONR^{20}R^{23}$ [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, $C_{1\text{-}8}$alkyl, aryl, and heteroaryl, which alkyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl or heteroaryl amide, CN, O-$C_{1\text{-}6}$ alkyl, CF_3;

R^{21} is a member selected from the group consisting of $C_{1\text{-}8}$ alkyl, aryl, and heteroaryl, which alkyl, aryl, and heteroaryl are optionally substituted with 1 to 2 substituents independently selected from the group of halo, CF_3, CN, OR^{20}, SR^{20},

$N(R^{20})_2$, $S(O)R^{22}$, SO_2R^{22}, $SO_2N(R^{20})_2$, $NR^{20}CO_2R^{22}$, $NR^{20}CON(R^{20})_2$, COR^{20}, CO_2R^{20}, $CON(R^{20})_2$, $NR^{20}SO_2R^{22}$, OR^{20}; and

R^{22} is a member selected from the group consisting of C_{1-8} alkyl, aryl, and heteroaryl, which alkyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl or heteroaryl amide, CN, O-C_{1-6} alkyl, CF_3, aryl, and heteroaryl.

55. (Once amended) The 2,6,9-trisubstituted purine composition of claim 52 wherein R_1' is selected from the group consisting of substituted aralkyl, aralkyl, substituted heteroarylalkyl and heteroarylalkyl.

57. (Once amended) A 2,6,9-trisubstituted purine composition of claim 54 wherein:

R'_1 is an aryl, heteroaryl, heterocyclyl, aralkyl, heteroarylalkyl, each having one to 20 carbon atoms, which aryl, heteroaryl, heterocyclyl, aralkyl, heteroarylalkyl, are optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, CF_3, aryl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, and $CONR^{20}R^{23}$;

R_2 is a hydrogen or hydrocarbon selected from the group substituted lower alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl each having one to 10 carbon atoms wherein substitution includes optional substitution with from 1 to 2 substituents independently selected from the group consisting of halo, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $NR^{20}R^{23}$, OR^{20}, and CN;

R_4 and R_5 are each independently hydrogen, or a hydrocarbon selected from the group [including]consisting of alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, alkenyl,

and alkynyl, each having one to 20 carbon atoms, which alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, alkenyl, and alkynyl, are optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, aryl, R^{22}, SR^{20}, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, and $CONR^{20}R^{23}$ [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, C_{1-8}alkyl, which alkyl is optionally substituted with 1 to 2 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or CN, O-C_{1-6} alkyl, CF_3;

R^{21} is a member selected from the group consisting of C_{1-8} alkyl, which alkyl is optionally substituted with 1 to 2 substituents independently selected from the group of halo, CF_3, CN, OR^{20}, SR^{20}, $N(R^{20})_2$; and

R^{22} is a member selected from the group consisting of C_{1-3}alkyl, aryl, heteroaryl which alkyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl, CN, O-C_{1-6} alkyl, CF_3.

58. (Once amended) The 2,6,9-trisubstituted purine composition of claim 52 wherein R_1' is selected from the group consisting of aryl, heterocyclyl, heteroaryl, and substituted heteroaryl[, and substituted aryl].

59. (Once amended) The 2,6,9-trisubstituted purine composition of claim 52 wherein R_1' is selected from the group consisting of aryl, unsubstituted pyridyl, and substituted pyridyl[, and substituted aryl], and R_2 is selected from the group consisting of alkyl, substituted alkyl.

60. (Once amended) The 2,6,9-trisubstituted purine composition of claim 51

wherein R_4 and R_5 are each selected from the group consisting of hydrogen, alkyl, heterocyclyl, acyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkyl alkenyl, alkyl alkynyl, each having one to 20 carbon atoms, which alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaryalkyl, are optionally substituted with from 1 to 3 substituents independently selected from the group consisting of halo, aryl, heteroaryl, heterocyclyl, R^{22}, SR^{20}, $S(O)R^{21}$, SO_2R^{21}, $SO_2NR^{20}R^{23}$, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}CONR^{20}R^{23}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, $CONR^{20}R^{23}$, and COR_{20} [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$].

61. (Once amended) A 2,6,9-trisubstituted purine composition of claim 60 wherein:

R'_1 is an aryl[, substituted aryl, each] having 6 carbon atoms[wherein substitution includes optional substitution with from 1 to 2 substituents independently selected from the group consisting of halo, CF_3, aryl, R^{22}, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, OR^{20}, CN];

R_2 is a hydrogen or hydrocarbon selected from the group consisting of substituted lower alkyl, cycloalkyl, and substituted cycloalkyl each having one to 6 carbon atoms wherein [substitution includes optional substitution] the substituted lower alkyl and substituted cycloalkyl are substituted with from 1 to 2 substituents independently selected from the group consisting of halo, R^{22}, $NR^{20}R^{23}$, OR^{20};

R_4 and R_5 are each independently hydrogen, or a hydrocarbon selected from the group [including]consisting of alkyl, and heterocyclyl wherein each hydrocarbon has from 1 to 12 carbon atoms, which alkyl, and heterocyclyl are optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, R^{22},

SR^{20}, OR^{20}, $NR^{20}R^{23}$, CN, CO_2R^{20}, and $CONR^{20}R^{23}$ [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, C_{1-8}alkyl;

R^{21} is a member selected from the group consisting of C_{1-3} alkyl, which alkyl is optionally substituted with 1 to 2 substituents independently selected from the group of halo, CF_3, CN, OR^{20}, SR^{20}, $N(R^{20})_2$; and

R^{22} is a member selected from the group consisting of C_{1-3}alkyl, aryl, heteroaryl which alkyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl, CN, O-C_{1-6} alkyl, CF_3.

62. (Once amended) A 2,6,9-trisubstituted purine composition of claim 60 wherein:

R'_1 is an aryl[, substituted aryl, each] having 6 carbon atoms [wherein substitution includes optional substitution with from 1 to 2 substituents independently selected from the group consisting of halo, CF_3, R^{22}, OR^{20}, CN];

R_2 is isopropyl;

R_4 and R_5 are each independently hydrogen, or a hydrocarbon selected from the group [including]consisting of alkyl, and heterocyclyl wherein each hydrocarbon has from 1 to 12 carbon atoms, which alkyl, and heterocyclyl are optionally substituted with from 1 substituent independently selected from the group consisting of R^{22}, OR^{20}, $NR^{20}R^{23}$ [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, C_{1-2}alkyl;

R^{21} is a member selected from the group consisting of C_{1-3} alkyl;

R^{22} is a member selected from the group consisting of C_{1-3}alkyl, aryl, which alkyl, aryl, are optionally substituted with 1 substituent independently selected from halo, alkyl, mono- or dialkylamino, CN, CF_3; and

R^{23} is R^{21} or H.

63. (Once amended) A 2,6,9-trisubstituted purine composition of claim 60 wherein:

R'_1 is an aralkyl, substituted aralkyl, each having 6-8 carbon atoms wherein substitution includes optional substitution with from 1 to 2 substituents independently selected from the group consisting of halo, CF_3, aryl, R^{22}, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, OR^{20}, CN;

R_2 is a hydrogen or hydrocarbon selected from the group substituted alkyl, cycloalkyl, substituted cycloalkyl each having one to 6 carbon atoms wherein substitution includes optional substitution with [from] 1 substituent independently selected from the group consisting of halo, R^{22}, $NR^{20}R^{23}$, OR^{20};

R_4 and R_5 are each independently hydrogen, or a hydrocarbon selected from the group [including]consisting of alkyl and heterocyclyl wherein each hydrocarbon has from 1 to 12 carbon atoms, which alkyl and heterocyclyl are optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, R^{22}, SR^{20}, OR^{20} ,$NR^{20}R^{23}$, CN, CO_2R^{20}, and $CONR^{20}R^{23}$ [$CONR^{20}R^2$ with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, C_{1-8}alkyl;

R^{21} is a member selected from the group consisting of C_{1-3} alkyl, which alkyl is optionally substituted with 1 to 2 substituents independently selected from the group of halo, CF_3, CN, OR^{20}, SR^{20}, $N(R^{20})_2$; and

R^{22} is a member selected from the group consisting of C_{1-3}alkyl, aryl, heteroaryl which alkyl, aryl, and heteroaryl are optionally substituted with 1 to 3 substituents independently selected from halo, alkyl, mono- or dialkylamino, alkyl or aryl, CN, O-C_{1-6} alkyl, CF_3.

64. (Once amended) A 2,6,9-trisubstituted purine composition of claim 60 wherein:

R'_1 is $-CH_2-$phenyl wherein the phenyl ring is optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, CF_3, R^{22}, OR^{20}, CN;

R_2 is isopropyl;

R_4 and R_5 are each independently hydrogen, or a hydrocarbon selected from the group [including]consisting of alkyl, and heterocyclyl wherein each hydrocarbon has from 1 to 12 carbon atoms, which alkyl, and heterocyclyl are optionally substituted with from 1 to 2 substituents independently selected from the group consisting of R^{22}, OR^{20}, $NR^{20}R^{23}$ [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, C_{1-2}alkyl;

R^{21} is a member selected from the group consisting of C_{1-3} alkyl;

R^{22} is a member selected from the group consisting of C_{1-3}alkyl, aryl, which alkyl, aryl, are optionally substituted with 1 substituent independently selected from halo, alkyl, mono- or dialkylamino, CN, CF_3; and

R^{23} is R^{21} or H.

65. (Once amended) The 2,6,9-trisubstituted purine composition of claim 60 wherein R_1' is selected from the group consisting of aralkyl, substituted pyridylalkyl, and unsubstituted pyridylalkyl;

R_2 is selected from the group consisting of alkyl, which alkyl is optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, R^{22}, $NR^{20}R^{23}$, OR^{20};

R_4 is a substituted alkyl having from 2 to 6 carbon atoms optionally substituted with from 1 to 3 substituents independently selected from the group consisting of R^{22}, OR^{20} , $NR^{20}R^{23}$;

R_5 is selected from the group consisting of hydrogen, alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, each having one to 20 carbon atoms, which alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, are optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, aryl, R^{22}, SR^{20}, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, and $CONR^{20}R^{23}$ [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, C_{1-2} alkyl;

R^{21} is a member selected from the group consisting of C_{1-3} alkyl;

R^{22} is a member selected from the group consisting of C_{1-3} alkyl, aryl, which alkyl, aryl, are optionally substituted with 1 substituent independently selected from halo, alkyl, mono- or dialkylamino, CN, CF_3; and

R^{23} is R^{21} or H.

66. (Once amended) The 2,6,9-trisubstituted purine composition of claim 60

wherein R_1' is selected from the group consisting of aryl, [substituted aryl,]pyridyl, and substituted pyridyl;

R_2 is selected from the group consisting of alkyl, which alkyl is optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, R^{22}, $NR^{20}R^{23}$, OR^{20};

R_4 is a substituted alkyl having from 2 to 6 carbon atoms optionally substituted with from 1 to 3 substituents independently selected from the group consisting of R^{22}, OR^{20} , $NR^{20}R^{23}$;

R_5 is selected from the group consisting of hydrogen, alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, each having one to 20 carbon atoms, which alkyl, acyl, heterocyclyl, aryl, heteroaryl, aralkyl, are optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, aryl, R^{22}, SR^{20}, $NR^{20}R^{23}$, $NR^{20}COR^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}SO_2R^{21}$, OR^{20}, CN, CO_2R^{20}, and $CONR^{20}R^{23}$ [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, C_{1-2} alkyl;

R^{21} is a member selected from the group consisting of C_{1-3} alkyl;

R^{22} is a member selected from the group consisting of C_{1-3} alkyl, aryl, which alkyl, aryl, are optionally substituted with 1 substituent independently selected from halo, alkyl, mono- or dialkylamino, CN, CF_3; and

R^{23} is R^{21} or H.

67. (Once amended) The 2,6,9-trisubstituted purine composition of claim 60 wherein R_1' is selected from the group consisting of aralkyl, pyridylalkyl, and substituted pyridylalkyl;

R_2 is selected from the group consisting of alkyl, which alkyl is optionally substituted with from 1 to 2 substituents independently selected from the group consisting of halo, R^{22}, and OR^{20};

R_4 and R_5 are each alkyl having from 2 to 6 carbon atoms substituted with 1 substituent independently selected from the group consisting of R^{22}, $NR^{20}R^{23}$, and OR^{20} [with the proviso that either R_4 or R_5 must be substituted with $NR_{20}R_{23}$];

R^{20} is a member selected from the group consisting of H, C_{1-2} alkyl;

R^{21} is a member selected from the group consisting of C_{1-3} alkyl;

R^{22} is a member selected from the group consisting of C_{1-3} alkyl; and

R^{23} is R^{21} or H.

72. (Once amended) The 2,6,9-trisubstituted purine composition of claim 60 wherein R_1' is selected from the group consisting of aryl[, substituted aryl,] pyridyl, and substituted pyridyl, R_2 is selected from the group consisting of lower alkyl, substituted lower alkyl, and alkyl cycloalkyl, and R_4 and R_5 are each a substituted lower alkyl having from 2 to 6 carbon atoms.

76. (Once amended) The 2,6,9-trisubstuted purine composition of claim 50 selected from the group consisting of [2-{(2-hydroxyethyl)[9-(methylethyl)-6-({[4-(trifluoromethyl)phenyl]methyl}amino)purin-2-yl]amino}ethan-1-ol,] {((2S)oxolan-2-yl)methyl](6-{[(4-fluorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)amine, [((2R)oxolan-2-yl)methyl](6-{[(4-fluorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)amine, (2-aminoethyl)(6-{[3,5-dichlorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)amine, (2-aminoethyl)[6-({[4-chloro-3-(trifluoromethyl)phenyl]methyl}amino)-9-

(methylethyl)purin-2-yl]amine, [-[(6-{[(4-chlorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)amino]-3-methylbutanamide, (2-amino-2-methylpropyl)(6-{[(4-chlorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)amine, 3-(2-[bis(2-hydroxyethyl)amino]-6-{[4-chlorophenyl)methyl]amino}purin-9-yl)butan-2-one, 2-[(6-{[(4-chlorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)amino]-3-methylbutan-1-ol, 4-[({2-[(2-aminoethyl)amino]-9-(methylethyl)purin-6-yl}amino)methyl]benzenesulfonamide, [2-[(2-hydroxyethyl)(6-{[(4-methoxyphenyl)methyl]amino}-9-(methylethyl)purin-2-yl)amino]ethan-1-ol,] [2-((2-hydroxyethyl){9-(methylethyl)-6-[(4-phenylphenyl)amino]purin-2-yl}amino)ethan-1-ol,] {2-[(2-amino-2-propyl)amino]-9-(methylethyl)purin-6-yl}[(4-chlorophenyl)methyl]amine, {2-[(2-aminoethyl)amino]-9-(methylethyl)purin-6-yl}[(4-chlorophenyl)methyl]amine, {2-[(2-aminopropyl)amino]-9-(methylethyl)purin-6-yl}[(4-chlorophenyl)methyl]amine and 2-[(2-aminoethyl)(6-{[(4-chlorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)amino]ethan-1-ol.

78. (Once amended) The 2,6,9-trisubstituted purine composition of claim [77] 60 wherein R_1' is selected from the group of compounds consisting of [4-methoxybenzyl,] 4-phenylbenzyl, 4-methoxybenzyl, 4-biphenyl, 3-methoxybenzyl, 4-(2-thienyl)benzyl, 4-(4-methyl)phenylbenzyl, 4-(4-trifluoromethyl)phenylbenzyl, 4-(4-nitrilo)phenylbenzyl, 4-(2-pyridinyl)benzyl, piperonyl, 3-thiomethoxphenyl, 4-thiomethoxyphenyl and 4-bromophenyl.

81. (Once amended) A method for treating a disease in a mammal that is characterized by abnormal cell proliferation [inhibiting cell proliferation in mammals]

comprising administering a therapeutically effective amount of the composition of claim 50 to the mammal.